

64. (New) A method according to claim 62, wherein the hydroxylamine has the general formula,



wherein R₁, R₂ and R₃ are independently selected from: hydrogen, substituted or unsubstituted (C1-C10) alkyl, alkenyl, alkynyl, aryl, oxyl, acyl, carboxyl, amino, nitro, nitroso, oxime, hydrazone, azo, thiol, sulfonyl and halide.

65. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is selected from unsubstituted (C1-C10) alkyl, alkenyl and alkynyl.

66. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is selected from unsubstituted (C1-C18) alkyl, cycloalkyl, alkenyl and alkynyl, and the R is selected from: CH₃-(CH₂)_{n1}, (CH₃-(CH₂)_{n2}-)₂ CH, (CH₃-(CH₂)_{n2}-)₃, cyclopentyl, cyclohexyl, (CH₂=CH-CH₂)_{n3} and (CH₂=C-CH₂-)_{n3}, wherein n1 = 1 to 18, n2 = 1 to 17 and n3 = 1 to 3.

67. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is selected from hydrogen, unsubstituted (C1-C10) alkyl, alkenyl and alkynyl, and the hydroxylamine is selected from:

N-methylhydroxylamine,
N-ethylhydroxylamine,
N-n-propylhydroxylamine,
N-(n-butyl) hydroxylamine,
N-(n-pentyl)hydroxylamine,
N-(n-hexyl)hydroxylamine,
N-(n-heptyl)hydroxylamine,
N-(n-octyl)hydroxylamine,
N-(n-nonyl)hydroxylamine,
N-(n-decyl)hydroxylamine,
N-(n-dodecyl)hydroxylamine,

N-(n-decahexyl)hydroxylamine,
N-(n-decaoctyl)hydroxylamine,
N-isopropylhydroxylamine,
N-sec-butylhydroxylamine,
N-tert-butylhydroxylamine,
N-cyclohexylhydroxylamine,
N-cyclopentylhydroxylamine,
N-(2-propene)hydroxylamine,
N-(3-butene)hydroxylamine,
N-(2-propyne)hydroxylamine and
N-(3-butyne)hydroxylamine.

68. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl.

69. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the R is selected from: mono, di, or tri methyl, methoxy, halo, nitro, amino, hydroxyl and substituted or unsubstituted phenyl, naphthyl, anthryl, phenanthryl, pyridyl, quinolinyl, imidazolyl, benzoxazolyl, pyrrolyl, furanyl, piperidinolyl and tetrahydrofuranolyl.

70. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the hydroxylamine is selected from:

N-benzylhydroxylamine, N-(1,3-diaminobenzyl)hydroxylamine,
N-(n-nitrobenzyl)hydroxylamine, N-(1,3-hydroxybenzyl)hydroxylamine,
N-(n-methylbenzyl)hydroxylamine, N-(2,4-diaminobenzyl)hydroxylamine,
N-(n-chlorobenzyl)hydroxylamine, N-(2,4-dihydroxybenzyl)hydroxylamine,
N-(n-aminobenzyl)hydroxylamine, Imidazole-2-methylhydroxylamine and
N-(n-hydroxybenzyl)hydroxylamine, Benzoxazole-2-methylhydroxylamine,

wherein n is selected from 1, 2, 3, 4, 5 and 6.

71. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxyl.

72. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxyl and the R is selected from: hydroxyl, hydroxyalkyl (HO-(CH₂)_{n1}), hydroxyaryl selected from benzylalcohol, phenol and naphthol, alkoxy (O-(CH₂)_{n1}) and aryloxy selected from phenoxy, benzyloxy and naphthyoxy, wherein n1= 1 to 18.

73. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18)alkyl hydroxyl or arylhydroxyl and the hydroxylamine is selected from:

N-(hydroxymethyl)hydroxylamine,
N-(2-hydroxyethyl)hydroxylamine,
N-(3-hydroxypropyl)hydroxylamine,
N-(4-hydroxybutyl)hydroxylamine,
N-(6-hydroxyhexyl)hydroxylamine,
N-(12-hydroxydodecyl)hydroxylamine,

N-(methoxymethyl)hydroxylamine,
N-(methoxyethyl)hydroxylamine,
N-(methoxyisopropyl)hydroxylamine,
N-(benzyloxymethyl)hydroxylamine and
N-(4-hydroxymethylbenzyl)hydroxylamine.

74. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkylcarboxyl or arylcarboxyl.

75. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkyl or aryl carboxyl and the R is selected from carboxyalkyls and benzyl.

76. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarboxyl and the hydroxylamine is selected from:

N-(carboxymethyl)hydroxylamine,
N-(2-carboxyethyl)hydroxylamine,
N-(3-carboxypropyl)hydroxylamine,
N-(4-carboxybutyl)hydroxylamine,

N-(5-carboxypentyl) hydroxylamine,
N-(6-carboxyhexyl)hydroxylamine,
N-(4-carboxybenzyl)hydroxylamine and
N-(12-carboxydodecyl)hydroxylamine.

77. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) ester.

78. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) ester and the R is selected from alkyl (C1 – C18) and aryl esters.

79. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylesters and the hydroxylamine is selected from:
N-(acetyloxymethyl)hydroxylamine,

N-(acetyloxyethyl)hydroxylamine,
N-(acetyloxypropyl)hydroxylamine,
N-(propylcarbonyloxy)methylhydroxylamine,
N-(butylcarboxyloxy)methylhydroxylamine,
N-(tert-butyloxycarboxyl)methylhydroxylamine,
N-(benzyloxycarbonyl)methylhydroxylamine,
N-(phenyloxycarbonyl)methylhydroxylamine,
N-(3-pyridyloxycarbonyl)methylhydroxylamine and
N-(benzoxazol-5-carbonyloxy)methylhydroxylamine.

80. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) carbonyl.
81. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted carbonyl and the R is selected from alkyl (C1 – C18) carbonyls and aryl carbonyls.
82. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarbonyls and the hydroxylamine is selected from:
- | | |
|---------------------------------------|---|
| N-(acetyl)methylhydroxylamine, | N-(phenylcarbonyl)methylhydroxylamine and |
| N-(ethylcarbonyl)methylhydroxylamine, | N-(benzylcarbonyl)methylhydroxylamine. |
| N-(butylcarbonyl)methylhydroxylamine, | |
83. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl(C1-C18) or aryl amino.
84. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or aryl amino and the R is selected from primary alkyl amine selected from methylamine, ethylamine, propylamine, butylamine and hexylamine, secondary amine selected from dimethylamine, diethylamine and dipropylamine, tertiary amine selected from trimethyl and triethylamine, and quarternary amine selected from tetramethyl and

tetra-ethylammonium salts.

85. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl(C1-C18) or aryl amine and the hydroxylamine is selected from:
N-aminomethylhydroxylamine,
N-(2-aminoethyl)hydroxylamine,
N-(N-methylamino)methylhydroxylamine,
N-(N,N-dimethylamino)methylhydroxylamine,
N-(N,N,N-trimethylammonium)methylhydroxylamine,
N-(3-aminopropyl)hydroxylamine,
N-(6-aminohexyl)hydroxylamine,
N-(4-aminobenzyl)hydroxylamine,
Hydroxylamine -1-methylpyridinium and
Hydroxylamine-1-methylquinolinium.

86. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkyl or aryl nitro.

87. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl(C1-C18) or aryl nitro and the R is selected from alkynitro selected from nitromethyl, nitroethyl, nitropropyl, nitrobutyl, nitropentyl, nitrohexyl and nitrobenzyl, and arynitro selected from nitrophenyl and nitronaphthyl.

88. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or aryl nitro and the hydroxylamine is selected from:

N-(nitromethyl)hydroxylamine,	N-(5-nitropentyl)hydroxylamine,
N-(2-nitroethyl)hydroxylamine,	N-(6-nitrohexyl)hydroxylamine,
N-(3-nitropropyl)hydroxylamine,	N-(4-nitrobenzyl)hydroxylamine and
N-(4-nitrobutyl)hydroxylamine,	N-(2,4-dinitrobenzyl)hydroxylamine.

89. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso.

90. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso and the R is selected from aliphatic nitrosoamines and aromatic nitroso.

91. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted nitroso (C1-C18) and the hydroxylamine is selected from:
N-(N-methyl-N-nitroso-amino)methyl hydroxylamine,
N-(N-methyl-N-nitroso-2-amino)ethylhydroxylamine,
N-(N-methyl-N-nitroso-3-amino)propylhydroxylamine and
N-(p-nitroso)benzylhydroxylamine.

92. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted oxime.

93. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxime and the R is selected from: acetaldoxime, propionaldoxime, butanaldoxime and benzaldoxime.

94. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted oxime (C1-C18) and the hydroxylamine is selected from:

Acetaldoxime-3-hydroxylamine,	Butanaldoxime-5-hydroxylamine and
Propionaldoxime-4-hydroxylamine,	(4-benzaldoxime)1-methylhydroxylamine.

95. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C10) hydrazone.

96. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C10) hydrazone and the R is selected from: acetaldehyde hydrazone, propanaldehyde hydrozone, butanaldehyde hydrazone and phenylhydrazone.

97. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydrazone (C1-C10) and the hydroxylamine is selected from

1-hydroxylamine-acetaldehyde hydrazone,
1-hydroxylamine-propanaldehyde hydrazone,
1-hydroxylamine-butanaldehyde hydrazone
and
1-hydroxylamine-benzylaldehyde hydrazone.

98. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo.
99. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo and the R is selected from: azobenzene, p-(phenylazo)benzyl and p-diazobenzyl.

100. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo and the hydroxylamine is selected from:

N-(p-phenylazo)benzylhydroxylamine,
N-(p-diazobenzyl)hydroxylamine and
N-(p-methoxylphenylazo)benzylhydroxylamine.

101. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol.

102. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol and the R is selected from (C1-C18) alkylthiol selected from methyl, ethyl, propyl, butyl, pentyl and hexyl thiol, and arylthiol selected from thiophenol and benzylthiol.

103. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol and the hydroxylamine is selected from:

N-(thiomethyl)hydroxylamine, N-(3-thiopropyl)hydroxylamine and
N-(2-thioethyl)hydroxylamine, N-(p-sulphydryl)benzylhydroxylamine.

104. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid.

105. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid and the R is selected from methanesulfonic acid, ethanesulfonic acid, propanesulfonic acid, butanesulfonic acid and p-toluenesulfonic acid.

106. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid and the hydroxylamine is selected from:

1-hydroxylamine-methanesulfonic acid,
1-hydroxylamine-ethane-2-sulfonic acid,
1-hydroxylamine-propane-3-sulfonic acid,

1-hydroxylamine-butane-4-sulfonic acid and
N-(p-sulfonyl)hydroxylamine.

107. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is halide.

108. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is halide and the R is selected from F, Cl, Br and I.

109. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is halide and the hydroxylamine is selected from:

N-(chloromethyl)hydroxylamine,
N-(bromomethyl)hydroxylamine,
N-(2-chloroethyl)hydroxylamine,
N-(3-chloropropyl)hydroxylamine,

N-(4-chlorobutyl)hydroxylamine,
N-(p-chlorobenzyl)hydroxylamine,
N-(p-fluorobenzyl)hydroxylamine and
N-(p-iodobenzyl)hydroxylamine.

110. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine.

111. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine and R is selected from N-methylhydroxylamine, N-ethylhydroxylamine, N-propylhydroxylamine N-butylhydroxylamine, N-pentylhydroxylamine, and N-benzylhydroxylamine.

112. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is is

substituted or unsubstituted hydroxylamine and the hydroxylamine is selected from:

Bis-methylhydroxylamine,
Bis-(2-ethyl)hydroxylamine,

Bis-(3-propyl)hydroxylamine and
Bis-benzylhydroxylamine.

113. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester.

114. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the R is selected from:
dimethylphosphate, diethylphosphate, dipropylphosphate and benzylphosphate.

115. (New) A method according to claim 64, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the hydroxylamine is selected from:
di-hydroxylaminemethylphosphate ester,
mono-hydroxylaminemethylphosphate ester,
mono-(1-hydroxylamine)-ethyl-2-phosphate ester,
di-(1-hydroxylamine)-2-ethylphosphate ester,
di-(1-hydroxylamine)-3-propyl-phosphate ester,
mono-(hydroxylamine-benzyl-phosphate ester and
di-hydroxylamine-benzylphosphateester.

116. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce infarct volume in a rat permanent middle cerebral artery occlusion (MCAO) stroke model.

117. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to protect against amyloid β peptide-induced neuronal cell death.

118. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce inflammation caused by LPS and INF- γ in E16 rat cortical neuronal cells.

119. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce β -amyloid-induced increased release of interleukin-1 β in human monocyte THP-1 cells.

120. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to protect against amyloid β peptide-induced locomotor impairment in rats.

121. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce spatial learning deficit in rats caused by N-nitro-L-arginine.

122. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce induction of experimental allergic encephalomyelitis (EAE) by injection of myelin basic protein (MBP) peptides in rats.

123. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce weight loss resulting from injection of myelin basic protein (MBP) peptides in rats.

124. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce acquisition learning deficit in Fas mutated autoimmune mice.

125. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce neuron loss following brain ischemia and reperfusion injury in gerbils resulting from experimental bilateral carotid occlusion.

126. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce loss of temporal/spatial short term memory following brain ischemia and reperfusion injury in gerbils resulting from experimental bilateral carotid occlusion.

127. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce infarct volume following brain ischemia and reperfusion injury in gerbils resulting from experimental bilateral carotid occlusion.

128. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce lethality volume following brain ischemia and reperfusion injury in gerbils resulting from experimental bilateral carotid occlusion.
129. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce β AP-mediated inactivation of glutamine synthetase (GS) and creatine kinase (CK) in rat brain tissue extracts and in cultured hippocampal neurons and glia.
130. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to reduce oxidation-caused side effects of adriamycin anticancer therapy in mice, as measured by acute lethality.
131. (New) A method according to claim 62, wherein the method detects the ability of the hydroxylamine to delay senescence in IMR90 human lung fibroblasts.

REMARKS

Claims 63-115 provide the same limitations as do claims 1-53 issued in US Pat 6,455,589; support for the specific embodiments of claims 116-131 are found in Examples 4-26 of the Specification. These amendments introduce no new matter.

We petition for and authorize charging our Deposit Account No.19-0750 all necessary extensions of time. The Commissioner is authorized to charge any fees or credit any overcharges relating to this communication to our Dep. Acct. No.19-0750 (order B00-001-2).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP



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